

# Reactions Monitor

Rapid, comprehensive identification of all adverse drug experience reports from 1700 international medical journals, presented as either summaries or citations to produce a complete file

## Calcium folinate/fluorouracil

Gastrointestinal disorders: S

### incidence study

Patients with advanced colorectal cancer participating in a phase III trial received IV calcium folinate [calcium leucovorin] 25mg/m<sup>2</sup> over 10 min (low dose) or 500 mg/m<sup>2</sup> over 2 hours (high dose) and/or IV bolus of fluorouracil 600 mg/m<sup>2</sup> given 1 hour later. This schedule was repeated weekly for 6 weeks followed by a 2-week break.

Those patients receiving  $\geq 1$  course of therapy were evaluated and experienced severe (25%) or worse (13%) diarrhoea during high and low dose calcium folinate regimens, respectively. A group of patients aged 67-81 (median 73) years suffered fatal toxicity during the first cycle of therapy. This included severe diarrhoea and/or nausea and vomiting and neutropenia with associated fever in most and sepsis and concurrent stomatitis in some patients. All patients exhibited dehydration and some had abdominal distension and pain. The terminal event was acute renal failure in 3 patients, of whom 2 had haemorrhagic enterocolitis ( $n = 1$ ) or serosanguinous ascites, pleural effusion and gastric mucosal lesions (1). A further patient with hypotension, abdominal pain and tenderness had ileitis, duodenitis and oesophageal ulceration but recovered with hydration, parenteral hyperalimentation, antibiotics and transfusions. A separate phase III trial of the high dose calcium folinate and fluorouracil regimen caused diarrhoea requiring dose-reduction of fluorouracil in half of the patients and death in 1 patient.

The toxic enterocolitis observed with low and high dose calcium folinate in combination with fluorouracil ... **should serve to caution against the use of this combination outside the clinical research setting.'**

Grem JL, Shoemaker DD, Petrelli NJ, Douglas Jr Ho. Journal of Clinical Oncology 5: 1704, Oct 1987